REMARKS

This Amendment, filed in reply to the Office Action dated August 25, 2009, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 14-21 are currently under examination, and are rejected. Claim 14 is amended herewith to incorporate the subject matter of Claims 16 and 17 therein. Claims 18 and 21 are amended herewith solely to improve clarity and conciseness. Claims 16 and 17 are canceled herewith, without prejudice or disclaimer.

No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Claims 14, 15 and 18-21 are Patentable Under 35 U.S.C. § 103(a)

1. On page 3 of the Office Action, Claims 14-20 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over EP 1174148A1, of record, in view of U.S. 2003/0190316A1, of record, essentially for the reasons set forth in the Office Action mailed January 30, 2009.

In maintaining the rejection, the Examiner acknowledges consideration of the Rule 132 Declaration submitted by Applicants, and the remarks directed thereto. However, the Examiner contends that such are unpersuasive, for the following reasons.

First, while Applicants noted that the '148 publication teaches away from using a citrate buffer, the Examiner alleges that Applicants' assertion that higher antibody stability is observed in the phosphate buffer vis-à-vis the citrate buffer is "misleading." Although the Examiner acknowledges that Table 1 of the '148 publication summarizes two sets of results, based on incubation at either 40°C or 60°C, and acknowledges that this data evidences that phosphate

buffer showed higher stability vis-à-vis the citrate buffer at 40°C., the Examiner alleges that conversely, the data also demonstrate that the citrate buffer provides higher resistance to degradation than the phosphate buffer when the incubation temperature is 60°C. In drawing this interpretation, the Examiner points to "Inventive Ex. 2" (a sodium phosphate buffer) in Table 1 of the '148 publication, which allegedly shows no degradation at 40°C (as judged by 100% retention of antibody titer), but 19 % degradation at 60°C (as judged by 81% retention of antibody titer); the Examiner appears to derive the degradation value for the 60°C sample by calculating the difference in percent degradation between the 40°C and 60°C samples. Using similar methodology, the Examiner contends that the citrate buffer shows only 4% degradation at 60°C, because the difference in degradation between the 40°C and 60°C samples is 4% (*i.e.*, 81%-77%; see "Inventive Ex. 3"). The Examiner thus construes the data in Table 1 to demonstrate that, at 60°C, antibody degradation in the phosphate buffer is 19%, whereas it is only 4% in the citrate buffer. The Examiner contends that one of ordinary skill in the art would thus select the citrate buffer, rather than the phosphate buffer, to enhance antibody stability at higher temperatures.

Second, the Examiner appears to consider Applicants' Declaration evidence to be insufficient to overcome the rejection because the claimed formulation is allegedly "required to exhibit suppression of chemical degradation." Specially, the Examiner alleges that Applicants' Declaration evidence does not demonstrate unexpectedly superior inhibition of chemical degradation. Further, the Examiner appears to contend that the data proffered to support unexpected results is not commensurate with claim scope. Specifically, the Examiner contends that the Declaration evidence only demonstrates unexpected results of soluble association of antibody using a combination comprising the KM-871 antibody at a concentration of 2mg/ml,

glycine at a concentration of 23mg/ml, and citric acid at a concentration of 10mM, and at pH6, and because the instant claims do not specifically recite these conditions, sustaining the rejection is proper.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, Applicants note that Claims 16 and 17 are canceled herewith, mooting the rejection of these claims.

Turning to the substance of the rejection, particularly the remarks in the outstanding Office Action that allegedly justify sustaining the rejection, Applicants respectfully disagree with the Examiner's interpretation of the data in Table 1 of the '148 publication, and submit that, for the following reasons, those of ordinary skill in the art would not share such an interpretation.

First, although the Examiner alleges that Applicants' argument that the '148 publication teaches away from using the citrate buffer is "misleading", Applicants respectfully submit that this allegation is baseless, stemming entirely from the Examiner's own flawed analysis of the experimental data in the '148 publication; in sustaining the rejection, the Examiner contends that because the *difference* in titer between the citric acid and phosphate buffers following incubation at 40°C and 60°C is 4% and 19%, respectively, then the citric acid buffer is thus superior to the phosphate buffer for inhibiting antibody degradation at high temperature. However, such a strained interpretation of the data defies logic, and is contrary to the interpretation that those of ordinary skill in the art would reach; as would instantly be appreciated by those of ordinary skill in the pertinent art, the difference in titer of 4% between incubation at 40°C and 60°C in the citrate buffer is a reflection of the *inferior* stabilizing ability of the citric acid buffer vis-à-vis the

phosphate buffer at 40°C, **not** *superiority* of the citric acid buffer vis-à-vis the phosphate buffer at 60°C.

Indeed, those of ordinary skill in the art would instantly recognize that the proper comparison is between the loss in titer with the phosphate buffer at 60°C and the loss in titer with the citric acid buffer at 60°C. As can be seen from Table 1, and as would be recognized by those of ordinary skill in the art, the phosphate buffer is not only superior at 40°C, demonstrating 0% loss in titer vis-à-vis the 19% loss observed with the citric acid buffer, but it is also superior at 60°C, demonstrating 19% loss in titer vis-à-vis the 23% loss observed with the citric acid buffer. Thus, in direct contrast to the Examiner's assertion, antibodies in the citrate buffer of the '148 publication are not "more resistant to degradation at higher temperature [than those in the phosphate buffer]." Rather, those of ordinary skill in the art would instantly understand that antibodies in the phosphate buffer are more resistant to degradation at 40°C and 60°C, and as such, would not select, and would be taught away from using, the citrate buffer.

In view of the foregoing, the data in Table 1 of the '148 publication, and the arguments set forth in the paragraph bridging pages 8 and 9 of the response filed May 29, 2009 (which arguments are incorporated by reference herein as if fully set forth in their entirety), Applicants submit that in view of this teaching away alone, the presently claimed invention is nonobvious, and patentable, over the cited references.

Second, and independent of the above, Applicants strongly, but respectfully, disagree with the Examiner's assessment of the sufficiency of Applicants' showing of unexpected results to establish nonobviousness. Specifically, the rejection is sustained, at least in part, on the premise that because the instant claims recite that the claimed composition suppresses chemical degradation, a showing of unexpectedly superior suppression of chemical degradation is required

if Applicants wish to rely on unexpected results to rebut the rejection; the Examiner contends that Applicants' proffered data does not establish that the claimed composition exhibits unexpectedly superior suppression of chemical degradation, citing Table 2, column 3, of the Rule 132 Declaration, and thus concludes that Applicants showing of unexpected results is not sufficient to overcome the rejection.

However, Applicants respectfully point out that there exists no statutory requirement, or basis in settled law, that if a claim recites several properties for a composition, a finding of obviousness can only be rebutted by a showing of unexpected results by demonstrating *that each and every property* occurs to an unexpected extent. This is not the law. To the contrary, it is well-settled that evidence of unexpected superiority in just **one** of a spectrum of common properties may be sufficient to rebut a *prima facie* case obviousness. See *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987). Thus, even assuming *arguendo* that the record lacks such a showing, such a showing is not required; as demonstrated by Table 2, column 2, of the Rule 132 Declaration, Applicants have demonstrated unexpectedly superior results with regard to at least one other property, namely suppression of soluble associations of antibody, and previously pointed out on the record the clear practical significance of this unexpected result. Nevertheless, because unexpected results need not be recited in the claims, but rather, only need to be possessed by the subject matter of the claims,[2] Claim 14 is amended for sake of clarity to simply recite the components of the claimed composition.

[2] See, for example, *In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007); and *In re Chu*, 66 F.3d 292, 298-99, 36 USPQ2d 1089, 1094-95 (Fed. Cir. 1995).

Further, although the Examiner contends that Applicants' data proffered to support unexpected results is not persuasive because it is not commensurate with claim scope, such a contention appears to be based solely on the data proffered in Applicants' Rule 132 Declaration, which described an exemplary composition of the present invention, the KM-871 antibody in a buffer consisting of glycine at a concentration of 23mg/ml, and citric acid at a concentration of 10mM, pH6. However, Applicants submit that such a contention improperly disregards the complementary data in the specification, which collectively, demonstrate that the unexpectedly superior result of suppressing soluble associations of antibody occurs across a wide range of citric acid and glycine concentrations. For example, Table 9 establishes that this unexpected property is evident across a 500-fold range of citric acid concentration (*i.e.*, 0.1-50 mmol/L, see Formulations 18 and 20 in Table 9 of the specification as filed). Tables 3 and 9 experimentally demonstrate that this unexpected property occurs with glycine concentrations of 10-30mg/ml. Moreover, in the interest of advancing prosecution, and without acquiescing to the merits of the rejection, Claim 14 is amended herewith to incorporate the subject matter of Claims 16 and 17, thereby specifically reciting the above-ranges; as shown in Tables 3 and 9 of the specification as filed, Applicants have experimentally demonstrated the unexpected result at the minimum and maximum glycine and citrate concentrations encompassed by the claims as amended, and one of ordinary skill in the art would logically extend the probative value of Applicants' experimental data to the intervening concentrations, and to antibodies of other specificities. Applicants respectfully submit that the unexpected properties claimed by Applicants are probative of the nonobviousness of the presently claimed invention, and as such, the claims are not rendered obvious for this reason also.

Withdrawal of the rejection is respectfully requested.

2. On page 5 of the Office Action, Claim 21 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over EP 1174148 and U.S. Patent Application Pre-grant Publication No. 2003/0190316, as applied above in the rejection of Claims 14-20, and further in view of U.S. Patent No. 6,488,930, of record.

In making the rejection, the Examiner expressly indicates that the '148 and '316 publications are relied upon for the same reasons as in the rejection of Claims 14-20 under 35 U.S.C. § 103(a). However, the Examiner acknowledges that neither publication discloses a human antibody to CCR4. Nevertheless, the Examiner contends that, at the time of the invention, one of ordinary skill in the art would readily have employed the stabilizing formulation allegedly taught by the combination of the '148 and '316 publications, to stabilize an anti-CCR4 humanized antibody, as allegedly disclosed by the '930 Patent.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Because the '930 Patent merely discloses humanized anti-CCR4 antibodies, and does not disclose glycine or citric acid based stabilization formulas, much less antibody solutions that inhibit soluble associations of antibody, Applicants submit that Claim 21 is nonobvious, and patentable, over the cited references for the same reasons as presented in response to the rejection of Claims 14-20, discussed above.

Withdrawal of the rejection is respectfully requested.

3. On page 7 of the Office Action, Claim 21 is further rejected under 35 U.S.C. § 103(a) as allegedly being obvious over EP 1174148 and U.S. Patent Application Pregrant

Publication No. 2003/0190316, as applied above in the rejection of Claims 14-20, and further in view of U.S. Patent No. 6,437,098, of record.

In making the rejection, the Examiner expressly indicates that the '148 and '316 publications are relied upon for the same reasons as in the rejection of Claims 14-20 under 35 U.S.C. § 103(a). However, the Examiner acknowledges that neither publication discloses a human antibody to ganglioside GD3. Nevertheless, the Examiner contends that, at the time of the invention, one of ordinary skill in the art would readily have employed the stabilizing formulation allegedly taught by the combination of the '148 and '316 publications, to stabilize an anti-GD3 humanized antibody, as allegedly disclosed by the '098 Patent.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Because the '098 Patent merely discloses humanized anti-GD3 antibodies, and does not disclose glycine or citric acid based stabilization formulas, much less antibody solutions that inhibit soluble associations of antibody, Applicants submit that Claim 21 is nonobvious, and patentable, over the cited references for the same reasons as presented in response to the rejection of Claims 14-20, discussed above.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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